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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,130	06/22/2000	MICHAEL JOHN DUGGAN	1581.0580000	2901

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,130	DUGGAN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/7/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed November 7, 2003 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 63-70 are pending.

Applicants' amendment filed on November 7, 2003 is acknowledged, and applicants' response has been fully considered. Claims 1-62 have been cancelled. Thus, claims 63-70 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 103(a)

3. The previous rejection of claims 1, 4-12, 14, 20-41, 44-47, 50-54 and 57 under 35 U.S.C. 103(a) as being unpatentable over Foster *et al.* (WO 96/33273) taken with Sharon *et al.* (The FASEB Journal 4, 3198-3208 (1990)), is withdrawn in view of applicants' cancellation of the claim, and applicants' response at page 6 in the amendment filed November 7, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 63, 64, 67, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treating pain, comprising a galactose-binding lectin, a light (L) chain or a L-chain fragment of a clostridial neurotoxin comprising the proteolytic enzyme domain, and a translocation domain of a clostridial neurotoxin heavy (H)

chain, wherein the galactose-binding lectin, the L-chain or a L-chain fragment and the translocation domain of a clostridial neurotoxin H-chain are linked by a covalent bond, and wherein the lectin is a bacterial origin, or is contacted with a modifying chemical and retains an ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue, does not reasonably provide enablement for an agent for treating pain, comprising a conjugate of a galactose-binding lectin, a L-chain or a L-chain fragment of a clostridial neurotoxin comprising the proteolytic enzyme domain, and a translocation domain of a clostridial neurotoxin H-chain, wherein the lectin is obtained from *Bandeirea simplicifolia*, or the lectin has been contacted with an enzyme, or has an amino acid insertion, deletion, or substitution, and retains an ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 63, 64, 67, 69 and 70 encompass an agent for treating pain, comprising a conjugate of a galactose-binding lectin, a L-chain or a L-chain fragment of a clostridial neurotoxin comprising the proteolytic enzyme domain, and a translocation domain of a clostridial neurotoxin H-chain, wherein the lectin is obtained from *Bandeirea simplicifolia* (claim 63, 64), a bacterial origin (claim 63), has been contacted with an enzyme (claim 63, 67) or a modifying chemical (claim 63), or has an amino acid insertion, deletion, or substitution in the native lectin (claims 63, 69, 70). The specification indicates an agent comprising a galactose-binding lectin or a fragment of galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin H-chain, wherein the three

components are linked together, can reduce and prevent the transmission of pain signals from nociceptive afferents to projection neurons (page 4, line 17-page 5, line 10; page 9, line 28-page 10, line 33). There are no indicia that the present application enables the full scope in view of an agent comprising a conjugate of a galactose-binding lectin or a fragment of galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin H chain as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claim is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claim is broad and encompasses unspecified variants regarding the galactose-binding lectin contacted with an enzyme or having an amino acid insertion, deletion or substitution in the native sequence, which is not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The examples indicate a conjugate of LH_N/A with a lectin from Erythrina cristagalli (ExL), E. corallodendron (EcL) or Glycine max (SBA), and the activity of ExL- LH_N/A in an electrophysiological or a behavior model of pain (Examples 1-8), and there are no working

examples indicating an agent comprising a galactose-binding lectin from *Bandeirea simplicifolia*, or the lectin has been contacted with an enzyme, or has an amino acid insertion, deletion, or substitution in the native sequence.

(3). The state of the prior art and relative skill of those in the art:

The related art (Foster *et al.*, WO 96/33273) indicates an agent comprising LH_N and a lectin can reduce the transmission of pain signals from nociceptive afferents to projection neurons (page 7, lines 15-17). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the make/use of a galactose-binding lectin from *Bandeirea simplicifolia*, or the lectin being contacted with an enzyme, or having an amino acid insertion, deletion, or substitution in the native sequence to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to an agent for treating pain, comprising a conjugate of a galactose-binding lectin, a L-chain of a clostridial neurotoxin or a functional fragment thereof, and a translocation domain of a clostridial neurotoxin H-chain, wherein the lectin is obtained from *Bandeirea simplicifolia*, a bacterial origin, or has been contacted with an enzyme or a modifying chemical, or has an amino acid insertion, deletion, or substitution in the native sequence, and retains an ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue. The specification indicates that the galactose-binding lectins can be purified from the seeds of genus *Erythrina* or *Glycine max*, or from bacteria *Pseudomonas aeruginosa* (page 7, line 12-page 9, line 15); and the agent for treating pain can be prepared form

the lectin of *Erythrina* or *Glycine max,* a L-chain of a clostridial neurotoxin or a functional fragment thereof, and a translocation domain of a clostridial neurotoxin H-chain (Examples 1-8); or the agent can be expressed as a fusion protein from nucleic acid encoding an appropriate fragment of the galactose-binding lectin (page 10, line 1-9). However, the specification does not describe the make/use of a galactose-binding lectin from *Bandeirea simplicifolia*, a galactose-binding lectin treated with an enzyme, or having an amino acid insertion, deletion, or substitution in the native sequence. Furthermore, the specification has not identified any galactose-binding lectin, which is treated with an enzyme or modified by amino acid insertion, deletion or substitution, nor has demonstrated the effects of the agents comprising these lectins. Since the specification fails to provide sufficient teachings on the treated or modified lectins, it is necessary to have additional guidance and to carry out further experimentation for assessing the effect of the agent containing the treated or modified lectin.

(5). Predictability or unpredictability of the art:

The claim encompasses an agent for treating pain, comprising a conjugate of a galactose-binding lectin, a L-chain of a clostridial neurotoxin or a functional fragment thereof, and a translocation domain of a clostridial neurotoxin H-chain, however, the make/use of the agent containing the lectins from *Bandeirea simplicifolia*, contacted with an enzyme, or having an amino acid insertion, deletion, or substitution in the native sequence are not described in the specification, and the invention is highly unpredictable regarding the effect of the agent in treating pain.

(6). Nature of the Invention

The scope of the claim includes an agent for treating pain comprising a treated or modified galactose-binding lectin, but the specification does not identify the treated or modified galactose-binding lectin, nor demonstrate the effect of the agent. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of agent.

5. Claims 63, 64, 67, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 63, 64, 67, 69 and 70 are directed to an agent for treating pain, comprising a galactose-binding lectin, a L-chain or a L-chain fragment of a clostridial neurotoxin comprising the proteolytic enzyme domain, and a translocation domain of a clostridial neurotoxin H-chain, wherein the galactose-binding lectin, the L-chain or a L-chain fragment and the translocation domain of a clostridial neurotoxin H-chain are linked by a covalent bond, and the lectin is obtained from *Bandeirea simplicifolia* (claim 63, 64), a bacterial origin (claim 63), or has been contacted with an enzyme (claim 63, 67) or a modifying chemical (claim 63), or has an amino acid insertion, deletion, or substitution in the native sequence (claims 63, 69, 70), and retains an ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue. The specification indicates that galactose-binding lectin is a lectin

binds to oligosaccharide structures having a terminal residue of galactose or N-acetylgalactosamine, and lectins are found in various life forms, the most commonly sources are the seeds of plants, e.g., the galactose-binding lectins can be purified from the seeds of genus *Erythrina* or *Glycine max*, or from bacteria *Pseudomonas aeruginosa* (page 7, line 12-page 9, line 15); and the agent containing a galactose-binding lectin can be expressed as a fusion protein from nucleic acid encoding an appropriate fragment of the galactose-binding lectin (page 10, line 1-9). However, the specification does not describe an agent containing a galactose-binding lectin from *Bandeirea simplicifolia*, a galactose-binding lectin treated with an enzyme or a modified galactose-binding lectin and still retaining the ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue. Furthermore, the specification does not indicate what enzyme is used to treat the galactose-binding lectin, how the lectin is treated with an enzyme and remains functional, and what modification is carried out in the lectin sequence. There is no disclosure indicating the lectin, which is treated with an enzyme, or modified by amino acid insertion, deletion or substitution, is functional. Without guidance for structure to function/activity, one skilled in the art would not know which region or residue(s) of galactose-binding lectin is essential for function/activity and how to identify a functional galactose-binding lectin. The lack of a structure to function/activity relationship and the lack of representative species for the galactose-binding lectins obtained from *Bandeirea simplicifolia*, treated with an enzyme, or modified by amino acid insertion, deletion or substitution in the native sequence as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 63-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 63-70 are indefinite because of the use of the term "the lectin has an amino acid insertion, deletion, or substitution when compared with the polypeptide sequence of the corresponding native lectin protein". The term "the lectin has an amino acid insertion, deletion, or substitution when compared with the polypeptide sequence of the corresponding native lectin protein" renders the claim indefinite; it is unclear which amino acid has been deleted or substituted, where is the insertion in the sequence, and what amino acid sequence is obtained after modification. Claims 64-70 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

8. Claim 70 recites the limitation "the nucleic acid coding for the lectin protein" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 70 is also indefinite as to "the nucleic acid coding for the lectin protein has a nucleotide deletion, insertion or substitution when compared with the nucleic acid sequence coding for the corresponding native lectin protein", it is unclear what nucleotide has been deleted or substituted, where is the insertion in the sequence, and what nucleotide sequence is obtained after modification.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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January 21, 2004

ROBERT A. WAX
PRIMARY EXAMINER